REMARKS

This Amendment is submitted with a Request for Continued Examination in response to the final Office Action dated August 13, 2009 and subsequently issued Advisory Action dated December 22, 2009. Claims 6-7 are pending in this application. In the Advisory Action, the rejection of Claims 6 and 7 under 35 U.S.C. §102(a), §102(b) and §102(e) have been overcome. The rejection of Claims 6 and 7 under 35 U.S.C. §112, first paragraph, has been maintained. In response, Claim 6 has been amended. This amendment does not add new matter. A petition for a three month extension of time and a request for continued examination (RCE) is submitted herewith. The Director is authorized to charge $1,110.00 for the three month petition for extension of time and $810.00 for the RCE and any additional fees that may be required, or to credit any overpayment to Deposit Account No. 02-1818. If such a withdrawal is made, please indicate the Attorney Docket No. 3712036-00818 on the account statement. In view of the arguments set forth below, Applicants respectfully submit that the rejections should be withdrawn.

In the Office Action, Claims 6-7 are rejected under 35 U.S.C. §112, first paragraph, for failure to comply with the enablement requirement. In particular, the Patent Office asserts that neither the Specification nor the state of the art teaches that a composition which is targeted to and inhibits glucosylceramide synthase can treat and/or prevent any kind of epithelial tissue damage and thus it would require undue experimentation to practice the claimed invention. Applicants respectfully traverse this rejection for at least the reasons as set forth below.

It respectfully is submitted that the inquiry with respect to scope of enablement under 35 U.S.C. §112, first paragraph, is whether it would require undue experimentation to make and use the subject matter as claimed. The amount of experimentation that is permissible depends upon a consideration of all Wands factors, including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, and the breadth of the claims. *Ex parte Formann*, 230 USPQ 546 (Bd. Pat. App. & Int'f 1986); see also *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988).

As discussed in detail in previous responses, the instant Specification discloses a relationship between CD_{1d} expression and skin irritation/inflammation. For example, the present

Specification teaches that blocking or modifying CD_{1d} activity can be used to treat or prevent tissue damage by replacing damaged skin cells with "healthy" epithelial cells. See, Specification, page 5, lines 19-31. The Specification further teaches that the amount of glucosylceramide synthase transcripts may be reduced "such[] that they exert the desired effect [of blocking or modifying CD_{1d} activity] on the CD_{1d} molecule." See, Specification, page 9, lines 10-21. One of ordinary skill in the art would therefore understand that reducing the amount of glucosylceramide synthase blocks or modifies the activity of the CD_{1d} molecule and can be used to treat or prevent tissue damage.

Moreover, contrary to the Examiner's assertion above, Applicants submit that the state of the art at the time the instant application was filed was sufficient to enable one of skill in the art to practice the instant invention. In particular, Applicants provide herewith two journal publications which provide post filing evidence that the present invention was enabled at the time of filing for treating epithelial tissue damage by reducing glucosylceramide synthase via mRNA inhibition (*See, e.g.*, Deng *et al.* (2002) *Glycobiology* 12(3): 145-152 ("*Deng*"); and Struckhoff *et al.* (2004) *The Journal of Pharmacology and Experimental Therapeutics* 309(2): 523-532) ("*Struckhoff*"). For example, *Struckhoff* disclosed that ceramide levels in human specimens of primary and metastatic colon cancer contained approximately one-half the level of ceramide compared with respective normal colon mucosa from the same patient. Additionally, a number of multidrug resistant cell lines do not generate ceramide in response to therapy, suggesting that clinical manipulation of ceramide levels within tumors represents an important mechanism for decreasing both tumor survival and chemotherapeutics resistance. *Struckhoff* at page 524. Further, *Deng* disclosed that antisense transfection targeting the glucosylceramide synthase gene inhibited the synthesis of glucosylceramide — the direct product of glucosylceramide synthase and caused a striking reduction in melanoma formation in mice. *Deng* at page 145. Notably, *Deng* followed methods well within the scope and guidance of the present invention as disclosed at the time of filing. Therefore, *Struckhoff* and *Deng* serve as proper post filing evidence that the specification as filed enabled one of skill in the art to make and use the disclosed invention without undue experimentation.

Accordingly, for the above-mentioned reasons, Applicants respectfully request that the rejection of Claims 6-7 under 35 U.S.C. §112, first paragraph, for failure to comply with the enablement requirement, be reconsidered and withdrawn.

For the foregoing reasons, Applicants respectfully request reconsideration of the above-identified patent application and earnestly solicit an early allowance of same. In the event there remains any impediment to allowance of the claims which could be clarified in a telephonic interview, the Examiner is respectfully requested to initiate such an interview with the undersigned.

Respectfully submitted,

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